

WHAT IS CLAIMED IS:

1. A method of forming polymers having diverse monomer sequences on a single substrate, said substrate comprising a surface with a plurality of selected regions, said method comprising the steps of:

a) forming a plurality of channels adjacent said surface, said channels at least partially having a wall thereof defined by a portion of said selected regions;

b) placing selected monomers in said channels to synthesize polymers at said portion of said selected regions, said portion of said selected regions comprising polymers with a sequence of monomers different from polymers in at least one other of said selected regions; and

c) repeating steps a) and b) with said channels formed along a second portion of said selected regions.

2. The method as recited in claim 1 wherein said step of forming a plurality of channels comprises the step of placing a channel block adjacent said surface, said channel block having a plurality of grooves therein, walls of said grooves and said surface at least partially defining said flow channels.

3. The method as recited in claim 1 wherein the step of placing selected reagents in said channels comprises the steps of: removing a protecting group from an active site in at least a first channel;

flowing a first monomer through said at least a first channel, said first monomer comprising a protecting group thereon, said first monomer binding to said active site in said first channel;

removing a protecting group from said active site in at least a second channel, at least a portion of said second channel overlapping a portion of said substrate contacted by said first channel; and

flowing a second monomer through said at least a second channel, said second monomer binding to said active site in said second channel.

4. The method as recited in claim 1 further comprising the step of screening said polymers for binding affinity with a receptor.

5. The method as recited in claim 1 wherein at least 10 different polymers are formed on said surface.

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6. The method as recited in claim 1 wherein at least 1,000 different polymers are formed on said surface.

7. The method as recited in claim 1 wherein at least 100,000 different polymers are formed on said surface.

8. The method as recited in claim 1 wherein said polymers are selected from the group consisting of oligonucleotides and peptides.

9. The method as recited in claim 1 wherein said selected regions each have an area of less than about 10,000 microns<sup>2</sup>.

10. The method as recited in claim 3 wherein the steps of removing and flowing further comprise the steps of:  
placing a channel block in contact with said surface in a first orientation and placing a material comprising a first monomer through at least one channel in said channel block;

rotating one of said channel block and said substrate relative to the other; and

placing a channel block in contact with said surface in a second orientation and placing a material comprising a second monomer through at least one channel in said channel block.

11. The method as recited in claim 1 wherein said steps of placing selected reagents in said channels comprises:

placing a pipet in fluid communication with said channel;  
and

injecting said selected reagents through said channels.

12. The method as recited in claim 11 wherein said step of placing a pipet in fluid communication with said channel is a step of placing said pipet in contact with an orifice on a side of said substrate opposite said surface.

13. The method as recited in claim 11 wherein said step of placing a pipet in fluid communication with said channel is a step of placing a plurality of pipets in communication with a plurality of said channels and flowing different reagents through at least two of said channels.

14. The method as recited in claim 1 preceded by the step of forming an array of valves of said surface whereby fluid may be directed to desired locations on said surface, and selectively

operating said valves and flowing said selected reagents through channels formed thereby.

15. The method as recited in claim 1 preceded by the step of irradiating portions of said substrate with light whereby photoremovable groups are removed from active groups on said substrate.

16. The method as recited in claim 15 wherein said selected irradiated portions are in the form of stripes, and wherein said step of forming channels comprises forming said channels along a path of said stripes, different reagents placed in at least a portion of said channels.

17. A method of forming a plurality of peptide sequences on a surface of a single substrate comprising the steps of:

a) placing said substrate in contact with a channel block in a first orientation, said channel block having a plurality of channels therein;

b) flowing at least a first amino acid through at least one of said channels, coupling said first to portions of said surface;

c) flowing at least a second amino acid through at least one of said channels, coupling said second amino acid to portions of said surface;

d) rotating said channel block relative to said substrate and placing said substrate in contact with said channel block again;

e) flowing a third amino acid through at least one of said channels to form at least first and second peptide sequences on said surface; and

f) flowing a fourth amino acid through at least one of said channels to form at least third and fourth peptide sequences on said surface.

18. A kit for forming diverse polymer sequences comprising:

a substrate;

a channel block, said channel block having a plurality of grooves therein;

means for holding said channel block in engagement with said substrate;

means for translating said channel block and said substrate relative to the other; and

means for injecting selected reagents into said grooves.

19. The kit as recited in claim 18 wherein said substrate comprises active site protecting groups.

5 20. The kit as recited in claim 19 further comprising a deprotecting material for removal of said protecting groups.

10 21. The kit as recited in claim 18 wherein said grooves are connected to apertures in said channel block, said apertures extending through a back surface of said substrate.

15 22. The kit as recited in claim 18 further comprising means for irradiating selected portions of said substrate for removal of protecting groups on said substrate, said protecting groups removed from active sites on said substrate upon exposure to light.

20 23. The kit as recited in claim 22 wherein said means for irradiating comprises a light source and a light mask, said light mask comprising regions opaque to said light and regions transmissive to said light.

24. The kit as recited in claim 18 wherein said means for injecting comprises a pipettor.

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25. The kit as recited in claim 24 wherein said pipettor comprises a plurality of pipettes, each of which is coupled to a different one of said grooves.

5 26. A system for conducting a plurality of reactions on a single substrate, the system comprising:

at least about 100 reaction regions on the single substrate, each reaction region being capable of conducting a separate reaction;

10 means for delivering one or more reactants to one or more of the reaction regions; and

means for constraining at least some of the reactants from contacting at least some of the reaction regions.

15 27. The system recited in claim 26 wherein the substrate comprises a plurality of passages and the reactions are supported within said passages.

20 28. The system recited in claim 26 wherein the means for delivering the one or more reactants are flow channels of a channel block adjacent the substrate and the means for constraining at least some of the reactants are walls of the flow channel.

25 29. The system recited in claim 26 wherein the means for constraining at least some of the reactants is a hydrophobic layer on the surface of the substrate.

30 30. A substrate comprising greater than about 100 reaction regions having different compounds therein; a constraining region surrounding the reaction regions, the constraining region being more hydrophobic than the reaction regions.

35 31. The substrate recited in claim 30, wherein the constraining region comprises hydrophobic protecting groups.

40 32. The substrate recited in claim 31 wherein the protecting groups are photolabile.

33. The substrate recited in claim 30 wherein the reaction regions define channels.

45 34. The substrate recited in claim 30 wherein the substrate includes greater than about 1000 reaction regions.

35. A method of forming a plurality of polymers having diverse monomer sequences on a substrate, the substrate including a plurality of reaction regions surrounded by a constraining region, the reaction regions being more wettable by one or more monomer solutions than the constraining region, the method comprising

sequentially placing the one more monomer solutions in a first reaction region to form a first polymer having a first monomer sequence, the monomer solutions being confined to the first reaction region by the constraining region; and

sequentially placing the one more monomer solutions in a second reaction region to form a second polymer having a second monomer sequence, the monomer solutions being confined to the first reaction region by the constraining region.

36. The method recited in claim 35 wherein the steps of placing monomer solutions in the first reaction region include moving a pipette with respect to the substrate and depositing at least one monomer solution in the first reaction region.

37. The method recited in claim 35 further comprising steps of periodically removing monomer solutions from the first and second reaction regions after selected monomers have been coupled to the first and second polymers.

38. The method recited in claim 35 wherein a first monomer is coupled in the first reaction region and a second monomer is coupled in the second reaction regions before additional monomers are placed and coupled in the first and second reaction regions.

39. The method recited in claim 35 wherein the monomer solutions are placed in the first and second reaction regions by a dispenser selected from the group consisting of an electrophoretic pump, a pipette, and a charged drop dispenser.

40. A method of transforming a first heterogeneous array of compounds on a single substrate, the heterogeneous array of compounds having a plurality of reaction regions, the method comprising the following steps:

activating a first group of  $r$  action regions and a second group of  $r$  action regions;

delivering a first reactant to the first group of  $r$  action regions and a second reactant to the second group of reaction regions;

allowing the first reactant to react at the first group of reaction regions, to convert the first heterogeneous array

into a second heterogeneous array, wherein the heterogeneous arrays have greater than about 100 distinct reaction regions.

41. The method recited in claim 40 further comprising a  
5 step of isolating the first group of reaction regions from the second group of reaction regions.

42. The method recited in claim 41 wherein the first  
10 group of reaction regions is isolated by placing a channel block against the substrate.

43. The method recited in claim 40 wherein the first  
15 group of reaction regions is isolated from the second group of reaction regions by walls on the substrate.

44. The method recited in claim 43 wherein the  
20 substrate includes a series of flow through reaction regions separated from one another by walls.

45. The method recited in claim 40 wherein the first  
25 group of reaction regions is isolated from the second group of reaction regions by one or more non-wetting regions on the substrate.

46. The method recited in claim 40 wherein the  
30 heterogeneous arrays have greater than about 1000 distinct reaction regions.

47. The method recited in claim 40 further comprising  
the following steps:  
35 delivering a second reactant to the second group of reaction regions but not to the first group of reaction regions;  
allowing the second reactant to react at the second group of reaction regions;  
activating a third group of reaction regions, the  
35 third group having some reaction regions in common with the first group of reaction regions;  
delivering a reactant to the third group or  
reaction regions but not to the second group of reaction regions; and  
40 allowing the a reaction to take place in the third group of reaction regions.

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